James R. Condo (#005867)
Amanda C. Sheridan (#027360)
SNELL & WILMER L.L.P.
One Arizona Center
400 E. Van Buren, Suite 1900
Phoenix, AZ 85004-2204
Telephone: (602) 382-6000
jcondo@swlaw.com
asheridan@swlaw.com

Richard B. North, Jr. (admitted *pro hac vice*)
Georgia Bar No. 545599
Matthew B. Lerner (admitted *pro hac vice*)
Georgia Bar No. 446986
NELSON MULLINS RILEY & SCARBOROUGH LLP
Atlantic Station
201 17th Street, NW, Suite 1700
Atlanta, GA 30363
Telephone: (404) 322-6000
richard.north@nelsonmullins.com
matthew.lerner@nelsonmullins.com

Attorneys for Defendants
C. R. Bard, Inc. and
Bard Peripheral Vascular, Inc.

IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF ARIZONA

IN RE: Bard IVC Filters Products Liability Litigation

No. 2:15-MD-02641-DGC

DEFENDANTS' C. R. BARD, INC. AND BARD PERIPHERAL VASCULAR, INC.'S MOTION TO EXCLUDE THE OPINIONS OF REBECCA BETENSKY, PH.D. AND MEMORANDUM OF LAW IN SUPPORT

(Assigned to the Honorable David G. Campbell)

(Oral Argument Requested)

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

MOTION

Defendants C. R. Bard, Inc. and Bard Peripheral Vascular, Inc. (collectively "Bard"), pursuant to Federal Rule of Evidence 702 and *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), move the Court to exclude expert opinion testimony from Plaintiffs' expert witness Rebecca Betensky, Ph.D. The grounds for this motion are more fully set forth in the memorandum of law below.

MEMORANDUM OF POINTS AND AUTHORITIES

I. Introduction.

Dr. Rebecca Betensky, a biostatistician, opines that there is a higher risk of adverse events for Bard's retrievable inferior vena cava filters ("IVC Filters") than for Bard's permanent Simon Nitinol® Filter ("SNF") based on her analysis of uncontrolled adverse event reports. Dr. Betensky applied unsubstantiated assumptions in her calculation, resulting in biased opinions that could just as easily reflect the substantial differences in the way adverse events are detected and reported between these two device types than any actual elevation in risk for the retrievable filters. Not only does she admittedly lack the technical and medical expertise to formulate the assumptions necessary for her opinions about these specialized products, but she also failed to collaborate with anyone possessing the requisite expertise as is her custom outside of the courtroom. Dr. Betensky's assumptions are simply impermissible *ipse dixit*, which cannot form the basis of admissible expert testimony. *See G.E. v. Joiner*, 522 U.S. 136, 146 (1997). Moreover, her opinions are fatally flawed because she failed to consider potential adverse events from the first ten years that the SNF was on the market, although she considered adverse events for each of the retrievable filters starting at market introduction. When confronted with this critical omission she admitted that the SNF data that she did not account for could invalidate her opinions entirely. Nor did she rule out plausible alternative explanations for the increased risk she estimated. Finally, her opinions are based solely on an improper comparison of anecdotal adverse event reports contrary to express guidance from the Food and Drug Administration ("FDA"). For these reasons, and as set

forth more fully below, the Court should exclude Dr. Betensky's opinions.

II. Factual Background.

A. There Are Significant Differences Between Bard's Permanent SNF Filter and Various Retrievable IVC Filters That Could Impact How Adverse Events Are Detected and Reported.

This case involves Bard's IVC Filters, which are implantable prescription medical devices. Bard marketed several IVC Filters for permanent and retrievable indications. Those involved in this MDL are: the permanent SNF and the retrievable Recovery®, G2®, G2® Express, G2®X, Eclipse®, Meridian®, and Denali® Filters (collectively, the "retrievable filters"). Bard's IVC Filters were developed to prevent large blood clots in the deep veins of the body (deep vein thrombosis or "DVT") from traveling to the lungs, causing pulmonary embolus, a well-recognized and leading cause of sudden death. The filters consists of two tiers of spokes that make up the "arms" and "legs." The filters are introduced into the IVC using a catheter via the femoral vein located in the groin or the jugular vein in the neck. Once a filter is deployed, its arms and legs open and anchor the filter in the walls of the IVC. The filter then acts to catch blood clots that could otherwise flow into the lungs.

There are significant differences between the permanent SNF and retrievable filters. The retrievable filters carry an important added benefit over the SNF in that they can be removed from the body percutaneously (through the skin) in a non-invasive procedure months or even years after placement. The SNF, on the other hand, was designed to remain in a patient's body in perpetuity. If removal ever became necessary the patient required an open, major surgery. Retrievable filters may therefore be used in certain populations of patients who would not otherwise elect to receive a permanent filter. For example, retrievable filters are often used prophylactically in some otherwise healthy trauma patients for a temporary period to protect against the risk of PE when a permanent filter is unnecessary.

The benefit of retrievability leads to potential differences in the frequency with which adverse events are detected in patients with retrievable filters relative to the SNF.

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

For example, it is well known that certain filter-related adverse events are asymptomatic, meaning that the patient does not feel or discern any symptoms associated with the problem. For patients with retrievable filters, these adverse events may first be detected when the filter is removed. In a similar patient with a permanent filter, the adverse event may never be detected. There are also potential differences in how frequently patients with permanent versus retrievable filters are followed. For example, patients with retrievable filters may be more closely followed than those with permanent filters as their physicians determine the appropriate time for filter removal. This could afford the patient more opportunities for certain asymptomatic adverse events to be detected than those with a permanent filter.

The length of time a filter remains in a given patient (dwell time) may also vary significantly between permanent and retrievable filters. Differences in dwell time between permanent and retrievable filters are not necessarily intuitive to those without expertise in these devices. Indeed, it cannot be said that permanent filters, as a rule, have longer dwell times than retrievable filters. An end-stage cancer patient may receive a permanent filter and subsequently pass away from the underlying disease shortly thereafter. Conversely, an otherwise healthy trauma patient may receive a retrievable filter that could remain in place for months or even years.

There are likewise differences between the retrievable filters and the SNF in the likelihood that an adverse event, once detected, will ever be reported. In her expert report, Dr. Betensky recognizes the "Weber Effect," in which "[i]ncreased reporting can be observed soon after the launch of a drug, and then decrease over time." (Betensky MDL Report, at 13, attached as Exhibit A.)[1] Reports generated by publicity, the so-called "notoriety effect" or "stimulated reporting" can also be observed for certain products. Dr. Betensky explained, "there's always a potential that there's increased reporting when a product first launches or that there's increased reporting surrounding some kind of

[1] Dr. Betensky's original and supplemental reports do not include page numbers. All citations to a page number should be read as if the report had been properly paginated.

notoriety." (Betensky Dep. Tr., at 110:11-14, July 26, 2016, ("Austin Dep. Tr.") attached as Exhibit B.)

Each of the retrievable filters came on the market long after the SNF was first available. Dr. Betensky considered reports of adverse events for the retrievable IVC filters starting at market launch for each product and continuing cumulatively forward. (*See* Betensky Dep. Tr., 116:22 to 117:4, June 23, 2017, ("MDL Dep. Tr.") attached as Exhibit C.) These were compared to reports for the SNF starting in the year 2000, although it was launched in 1990. (*See* Ex. A, MDL Rep., at 1.) Dr. Betensky thus omitted at least a decade of potential adverse event reports for the SNF from her calculations with unknown consequences to her ultimate opinions. (*See* Ex. C, MDL Dep. Tr., 120:25 to 122:13.)

B. Dr. Betensky's Analysis Involved the Application of Unfounded Assumptions to Improperly Compare MAUDE Data.

Plaintiffs retained Dr. Betensky to opine that Bard's retrievable filters have a higher risk of adverse events than Bard's SNF. (*See* Ex. A, MDL Rep., at 1, 14; *see also* Ex. C, MDL Dep. Tr., 172:18 to 173:5.) Dr. Betensky did not rely on any controlled data. Rather, she relied entirely on anecdotal adverse event reports. (*See* Ex. B, Austin Dep. Tr., 42:1-3 ("I just want to be clear that the basis of the analysis and the basis of the estimates are based on what is reported.").)

The reports were those either made directly to Bard or that Bard retrieved from the FDA's Manufacturer and User Facility Device Experience Database ("MAUDE"), a collection of medical device adverse event reports. MAUDE data has numerous well-known limitations. While manufacturers of medical devices are required to submit all reports concerning possible adverse events of which they are aware to MAUDE, reports from other sources, including doctors, patients, hospitals, and even attorneys are completely voluntary. As a result, reports in MAUDE may be duplicative because both a manufacturer and a separate individual may report the same event. These reports are uncontrolled and unconfirmed. In other words, there is no requirement that the event

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

described in the report verifiably occurred, much less in the manner in which it was reported. Despite these limitations, FDA recognizes certain value and utility of MAUDE data when used by manufacturers in their internal investigations and assessments of the adverse events reported for their devices. However, the FDA specifically warns on the MAUDE database homepage that "**MAUDE data is not intended to be used either to evaluate rates of adverse events or to compare adverse event occurrence rates across devices**" (emphasis added). (MAUDE website, at https://www.fda.gov/medicaldevices/deviceregulationandguidance/postmarketrequirements/reportingadverseevents/ucm127891.htm (last visited Aug. 8, 2017), attached as Exhibit D.) Dr. Betensky did not perform her own independent review of MAUDE for the information she relied on. (*See* Ex. B, Austin Dep. Tr., 15:19-21.) Nor did she independently review the information underlying any of the reports she considered. (*See id.* at 92:4 to 93:3.)

Dr. Betensky's risk estimation required a two-step analysis. First, she compared the proportions of adverse event reports for the various retrievable filters over sales to the proportions of adverse event reports for the SNF over SNF sales. (*See* Ex. A, MDL Rep., at 3.) She called the resulting calculation a reporting risk ratio ("RRR"). (*Id.*)

$$RRR = (x_1/n_1)/(x_2/n_2).$$[2]

Dr. Betensky emphasized that "the qualifier 'reported' is important and that's indicating that the data are coming from reports, and are not being derived from a beautifully run and designed experiment like a clinical trial, in which there's perfect follow-up and in which it's really a true experiment. So the 'reporting' qualifier is there to say and to suggest that these are numbers that are reported. These are based on reports." (Ex. B, Austin Dep. Tr., 60:12-20.) Because of the inherent limitations in the data that she considered, Dr. Betensky's RRR in and of itself does not quantify actual risk. Rather, it is "just an estimate" based on *unconfirmed reports* submitted either to Bard, MAUDE, or both. (*Id.*

[2] Ex. A, MDL Rep. at 3 (defining RRR when x_1 denotes the number of AE's for the product of interest, x_2 denotes the number of AE's for the SNF, n_1 denotes the total units sold for the product of interest and n_2 denotes the total units sold for SNF.).

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

at 113:21-23.)

Indeed, Dr. Betensky's RRR "could be an overestimate or it could be an underestimate" of risk, which is why it is not the true measure of interest in this case. (*Id.* 62:14-19.) Dr. Betensky described her RRR as a "crude estimate[] of risk." (*Id.* at 106:20-25.) According to Dr. Betensky, the risk ratio ("RR") is truly the "quantity of interest." (Betensky Thisted Rebuttal Report, at 1, attached as Exhibit E ("The reporting risk ratio, which is what can be estimated from available data, is informative about the risk ratio, which is the quantity of interest.").) Unlike Dr. Betensky's RRR, an actual RR would not be "entangled with issues around reporting." (Ex. B, Austin Dep. Tr., 60:21-25.)

Dr. Betensky recognized the analytical leap between the RRR she calculated and an estimation of RR. (*See id* at 134:25 to 135:14 ("So again, there's the . . . leap, . . . between the reporting rates or risks and the actual risks.").) Dr. Betensky, therefore, *estimated* RR in this case based on her RRR calculations. She did not calculate an actual quantifiable increased risk or numerical value for RR. She simply inferred that the RR was greater for the retrievable filters than for the SNF after considering her RRR calculations in light of what she determined were "some plausible assumptions on detection, reporting, and implantation of sold devices, in conjunction with consideration of serious adverse events." (Ex. E, Rebuttal Rep. at 1; *see also* Ex. C, MDL Dep. Tr., 96:9-11 ("in order to . . . draw inferences about the risk ratio from the reporting risk ratio, that's where assumptions are required.").) As set forth below, however, Dr. Betensky's assumptions are unsubstantiated. Dr. Betensky admits that she is not an expert in IVC filters and did not consult with any such expert in the process of determining the "plausible assumptions" she needed to render opinions about RR in this case. (*See* Ex. C, MDL Dep. Tr., 25:8-11; 187:16.)

III. Argument.

A. Dr. Betensky Admits She Is Not an IVC Filter Expert, and the Assumptions Necessary for Her Risk Ratio Estimation Are Impermissible *Ipse Dixit.*

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

Dr. Betensky did not do an apples-to-apples comparison. She did not analyze risk for adverse events between retrievable filters. Rather, she undertook an apples-to-oranges analysis, comparing adverse events in the permanent SNF to various retrievable IVC filters. If there are differences between the retrievable filters and the SNF in the way these adverse events are either detected or reported, "it wouldn't be appropriate to consider the reporting risk ratio as a risk ratio." (Ex. C, MDL Dep. Tr., 177:11-12.) Therefore, in order to draw unbiased inferences about RR from her RRR calculations, Dr. Betensky was "required" to apply certain "plausible" assumptions about the way in which adverse events are first detected and then reported in the SNF as opposed to the retrievable filters. If her assumptions are unfounded or wrong, that means her opinions on risk are biased. In other words, the elevated risk she calculated could be due to reasons totally unrelated to any *actual* increased risk. (*See* Dr. Thisted MDL Report, at ¶¶ 99, 109, 113, attached as Exhibit F.) It could be that doctors are more likely to report adverse events for the newer retrievable filters than for the SNF, which had been on the market for over a decade before the first retrievable filter was launched. (*See* Ex. A, MDL Rep., at 13.) Or for various reasons the adverse events at issue may be more easily detected in patients with retrievable filters. If so, and there are many reasons to think this is true, then there would be no elevated risk at all notwithstanding Dr. Betensky's calculations. (*See* Ex. F, Thisted Rep. at ¶ 114.)

Determining whether or not assumptions about detection and reporting of adverse events in retrievable and permanent filters are "plausible" requires an expert understanding of these complex medical devices and their use. Dr. Betensky, however, is not an IVC filter expert. (*See* C, MDL Dep. Tr., 187:16 ("I'm not a medical expert in these filters."); *see also* Ex. B, Austin Dep. Tr., 132:25 to 133:1 ("So I'm a statistician, I'm a statistical expert, I'm not a medical expert.").) She admits she has no expertise in the disciplines that might inform the various "plausible" assumptions she was "required" to apply to reach her RR opinions. She is not a medical doctor and does not treat patients. (*See* Ex. B, Austin Dep. Tr., 39:3-6.) She is not a radiologist. (*Id.* at 39:7-8.) Nor is she

an expert in human anatomy. (*Id.* at 39:9-12.) She is not an engineer. (*See* Ex. C, MDL Dep. Tr., 18:8.)

Specifically, Dr. Betensky disclaims the expertise necessary for her assumptions about the differences in detection and reporting of adverse events between the retrievable filters and the permanent SNF:

> Q. You're not a medical expert when it comes to what might impact the differential discovery and reporting of adverse events in a removable filter versus adverse events in a permanent filter?
>
> A. I'm not a medical expert in that.

(Ex. C, MDL Dep. Tr., 187:23 to 188:2.)

> Q. You're not an expert in the manner in which potential filter adverse events are detected, are you?
>
> A. Not in how they are clinically detected.

(*Id.* at 92:8-10.)

> Q. You're not an expert in the differences in how adverse events are clinically detected in retrievable filters versus permanent filters, right?
>
> A. Correct.

(*Id.* at 92:12-15.)

> Q. Do you hold yourself out as an expert in the FDA rules, regulations, and guidance related to submitting adverse event reports to MAUDE?
>
> A. I'm not an expert in those regulations.

(*Id.* at 93:8-11.)

Recognizing that she is not a medical doctor or expert in any specific scientific discipline other than statistics and related issues, in her non-litigation work she routinely collaborates with subject matter experts in the field. (*Id.* at 18:17-20 ("I have, you know, 25 years of experience as a Ph.D.-level statistician who has collaborated extensively with investigators in the medical field"); 19:16-22 ("Q. You often collaborate with subject matter experts in various fields of medicine when you publish an article, right? . . . A. I – yes, many of my . . . publications are collaborative publications with experts in medicine

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

and science."); 20:14-17 ("Q. And that's totally routine for you is what I'm driving at, right? A. I've, I've done it regularly over many years, yes."); 24:9-17 ("[W]ithin my department of biostatistics at the Harvard Chan School of Public Health, my colleagues, other faculty within that department and myself commonly collaborate with medical and public health and basic science experts in the development of both statistical methodology and in collaborative research, and everyone is usually an author -- a coauthor on the paper that comes out of that.").)

Yet in this case Dr. Betensky did not work with or collaborate with anyone. (*Id.* at 25:8-11.) Dr. Betensky's assumptions about differential detection and reporting of adverse events between the SNF and retrievable filters are not the product of her own expertise and do not come from anyone who purports to be an expert in this subject. Instead, they just seemed "reasonable" or "obvious" to her based on her "general understanding" of these complex devices:

> Q. . . . Who provided you the assumptions that you used?
>
> A. The assumptions are, in my view, reasonable assumptions based on, you know, my general understanding.
>
> Q. Your assumptions are not based on any medical expertise that you have with respect to these filters, right?
>
> A. I don't have medical expertise.

(*Id.* at 188:12-20.)

> Q. Did you consult or confer with anybody that has any medical expertise with respect to the products at issue to determine whether your assumption that the difference in reporting for the devices would be consistent?
>
> A. It seems obvious to me that, as long as the events are of comparable seriousness that that would follow.

(*Id.* at 108:23 to 109:6.)

> Q. Did you consult with anybody that has any medical expertise with respect to the adverse events at issue to determine whether your assumptions that the

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

> differential reporting -- whether your assumptions about differential reporting hold true?
>
> A. No.

(*Id.* at 109:9-14.)

Dr. Betensky recognized the "leap between the reporting rates or risks," the RRR she calculated, "and the actual risks," or RR she estimated. (Ex. B, Austin Dep. Tr., 134:25 to 135:14.) To bridge this analytical gap required her to apply assumptions about adverse event detection and reporting that are based on nothing more than her *ipse dixit* or say so. The Supreme Court squarely addressed this issue in *General Electric Company v. Joiner*, holding that "nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert. A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered." 522 U.S. 136, 146 (1997). The Court should likewise exclude Dr. Betensky's opinions in this case.

B. <u>Dr. Betensky's Opinions Should Be Excluded for Failure to Consider Necessary Data or Rule out Plausible Alternative Causes for the Elevated Risk She Estimated.</u>

As set forth above, Dr. Betensky compared the proportions of adverse event reports for the various retrievable filters over sales to the proportions of adverse event reports for the SNF over SNF sales. She considered adverse event reports and sales data for each of the retrievable filters starting at product launch. (*See* Ex. C, MDL Dep. Tr., 124:18-22.) For her comparison to the SNF, however, Dr. Betensky utilized adverse event reports and sales data starting in 2000 although she was aware that "the SNF was launched in 1990." (Ex. A, MDL Rep. at 13.) She therefore omitted the first ten years of adverse event reports and sales data from her analysis of the SNF. (*See* Ex. C, MDL Dep. Tr., 125:20 to 126:2 ("Q. In your analysis you captured periods in which the removal devices were new to the market, right? A. Yes. Q. In your analysis you didn't start considering adverse events for the Simon Nitinol filter until it had been on the market for over ten years, right? A. I believe that's true.").) This is particularly egregious considering that, under the

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

"Weber effect" that Dr. Betensky describes in her report, "[i]ncreased reporting can be observed soon after the launch of a drug." (Ex. A, MDL Rep. at 13.) Dr. Betensky thus failed to consider the period in which she would expect to find the most adverse event reports for the SNF.

Dr. Betensky's failure to include this decade-long span of adverse event and sales data for the SNF is fatal to her analysis. As she admitted, had she considered this missing data it is entirely possible that she would not have estimated *any* increased risk of adverse events for the removable filters:

> Q. Because you didn't have data for adverse events for SNF prior to 2000 and you didn't have sales data for SNF prior to 2000, there's no way for you, as you sit here today, to say that if you had that data and calculated reporting risk ratios perhaps the reporting risk ratios would be greater for SNF over removable, maybe they'd be lower. You just don't know one way or another, right?
>
> A. I don't have the data so I don't know what the number would be if I had had the data. It could go -- like you said, I could get -- I could have gotten RRs that are larger than what I got. I could have gotten RRs that are smaller than what I got.

(Ex. C, MDL Dep. Tr., 122:1-13.) Conceding the gravity of this obvious failure, Dr. Betensky admitted "So if I had had the data for the first ten years, I would have used it." (*Id.* at 189:21-22.)[3] Dr. Betensky's failure to consider pre-2000 data for the SNF admittedly invalidates her opinions, which the Court should exclude entirely.

Dr. Betensky likewise lacked the data to rule out plausible alternative causes for

[3] In a last-ditch effort to defend her analysis, Dr. Betensky speculated that her opinions might still have value as a comparison of current time periods because "although the SNF came on the market in 1990, perhaps other things have changed in medicine and in treatment of these patients who receive these filters and in, you know, ancillary treatments or drugs that are given to them alongside it or how surgery is conducted or any number of things that might have changed from 1990 to 2000. And so, that would be a reason why it might be more meaningful to compare . . . at the same time period given that . . . things in medicine do change quite a bit over ten years." (Ex. C, MDL Dep. Tr., 127:3-15.) Dr. Betensky had no idea, however, what if anything had actually changed for the devices and patients at issue. When asked what specific changes she was referring to, Dr. Betensky conceded "that would be something for a clinical expert to comment on." (*Id.* at 128:13-23.)

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

the increased risk she found. For example, she did nothing to account for the differences between the retrievable filters and the SNF when it comes to detecting asymptomatic adverse events. (*Id.* at 185:7-14 ("Q. What, if anything, did you do in this case to control for the possibility that individuals with asymptomatic adverse events that have retrievable filters only had those symptoms detected when the filter was removed? . . . A. I didn't have any information to do anything about that.").) Nor did she account for the fact that adverse event reports for the retrievable filters, including reports from plaintiff attorneys, might be increased due to ongoing litigation over those products and the attendant increased publicity that brings. (*Id.* at 189:7-10 ("A. I, I didn't take into account potential changes in reporting. Q. Based on litigation? A. Based on litigation."); 191:1-10 ("Q. It's entirely possible that the increases over time in reporting for the removable products that you noted were related to high profile litigation connected with the products, right? That's possible? . . . A. Anything is possible. I suppose. Q. You didn't do anything to rule out that possibility, did you? A. I don't have -- I didn't have the data to be able to do that kind of level of analysis.").

As set forth above, Dr. Betensky's failure to consider critical data invalidates her opinions that there is any increased risk for the retrievable filters over the SNF. Her opinions should therefore be excluded.

C. Dr. Betensky's Opinions Should Be Excluded Because They Result From Her Improper Comparison of Reporting Rates of Anecdotal Adverse Event Reports.

Dr. Betensky's opinions are inadmissible because they are based entirely on an improper comparison of reporting rates of anecdotal adverse event reports that were either made directly to Bard or that Bard retrieved from FDA's MAUDE Database. Although FDA recognizes certain value and utility of MAUDE data, its limitations and constraints are well known. Indeed, FDA states that the MAUDE database is a "passive surveillance system [that] has limitations, including the potential submission of incomplete, inaccurate, untimely, unverified, or biased data." (*See* MAUDE website, at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search.cfm#disclaimer (last

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

visited Aug. 8, 2017), attached as Exhibit G.) FDA further cautions that voluntary adverse event reporting systems, such as MAUDE, are subject to a variety of reporting biases and that data may be affected by the submission of incomplete or duplicate reports, underreporting, or reporting stimulated by publicity or litigation, leading to "substantial limitations in interpretation because of the inherent uncertainties in the numerator and denominator." (*See* FDA, Guidance for Industry: Good Pharmacovigilance Practices & Pharmacoepidemiologic Assessment, 2005 WL 3628217 § IV(G) (Mar. 2005), *available at* http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126834.pdf-title=Guidance (last visited Aug. 8, 2017), attached as Exhibit H.)

Because of these recognized limitations, courts have found that expert opinions that are based on comparative rates of case reports/adverse event reports, such as those found in the MAUDE database, are unreliable and therefore inadmissible because such reports are anecdotal "without any medical controls or scientific assessment." *See, e.g.*, *In re: Accutane Prods. Liab. Litig.*, 511 F. Supp. 2d 1288, 1298 (M.D. Fla. 2007) (excluding expert opinion based on adverse event reports and case reports because they "occurred without any medical controls or scientific assessment."); *see also Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194, 1199 (11th Cir. 2002) (affirming exclusion of expert opinion based on adverse event reports/case reports because they "reflect only reported data, not scientific methodology"); *Allison v. McGhan Medical Corp.*, 184 F.3d 1300, 1316 (11th Cir. 1999) (affirming exclusion of expert opinion based on case reports); *Haggerty v. Upjohn Co.*, 950 F. Supp. 1160, 1165 (S.D. Fla. Dec. 6, 1996), *aff'd* 158 F.3d 588 (11th Cir. 1998) (excluding expert opinion based upon adverse event reports and "anecdotal case reports appearing in medical literature" due to the "inherent bias" in the adverse event reports and that "while case reports may provide anecdotal support, they are no substitute for a scientifically designed and conducted inquiry"); *In re Denture Cream Prods. Liab. Litig.*, No. 09-2051-MD, 2015 WL 392021 (S.D. Fla. Jan. 28, 2015) (case reports are not a reliable basis for expert opinion); *In re Gadolinium-Based Contrast Agents Prod. Liab. Litig.*, No. 1:08 GD 50000, 2010 WL 1796334, at *11 (N.D. Ohio

May 4, 2010) (prohibiting expert opinion on comparative rates based solely on adverse event reports).

Dr. Betensky, readily admits the numerous limitations to MAUDE data. (*See* Ex. B, Austin Dep. Tr., 64:19 to 65:3 (recognizing "the messiness" in MAUDE data she used); 101:19-102:12 (underreporting a limitation); 102:15 to 103:11 ("So another limitation are data errors . . . . So anyway, there are many of these data errors."); 106:20-25 ("So another limitation is that these are crude estimates of risk."); 109:8-17 (recognizing data confounding due to patient-level characteristics); 110:9-14 (increased reporting due to notoriety or when product first launches).)

Because of the myriad limitations that Dr. Betensky identifies, the FDA specifically warns on the MAUDE database homepage that "**MAUDE data is not intended to be used either to evaluate rates of adverse events or to compare adverse event occurrence rates across devices**" (emphasis added). (Ex. D.) Indeed, Dr. Betensky quotes another warning from FDA's website which specifically provides that MAUDE "data alone **cannot be used to . . . compare event rates between devices**." (Ex. E, Rebuttal Rep., at 3.) Yet that is precisely how Dr. Betensky uses the MAUDE data. Contrary to FDA's admonition, Dr. Betensky misuses MAUDE to compare adverse event rates for Bard's retrievable filters against the SNF to highlight purported increased safety problems with the newer devices. Specifically, Dr. Betensky calculated "relative risks that were reported," in other words, "relative risks based on the frequency of complications reported in one filter versus another filter." (Ex. B, Austin Dep. Tr., 40:21-41:5.)

To be clear, Dr. Betensky did not calculate a true relative risk. She simply compared reporting rates, with all the attendant limitations, to create a so-called "reporting relative risk." As Dr. Betensky explained, "the qualifier 'reported' is important and that's indicating that the data are coming from reports, and are not being derived from a beautifully run and designed experiment like a clinical trial in which there's perfect follow-up and in which it's really a true experiment." (*Id.* at 60:12-17.) Yet, as

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000

Dr. Betensky admits, an actual relative risk (as opposed to the "reporting relative risk" she calculated) would have been the "target," and "is what would be of interest" because it is not "entangled with issues around reporting" unlike her calculations. (*Id.* at 60:21-25.)

FDA further warns that any comparisons of reporting rates across devices using MAUDE data should be "viewed with extreme caution and generally considered exploratory or **hypothesis-generating**." (Ex. H, FDA Guidance at § IV(G) (emphasis added).) Dr. Betensky directly quotes this warning in both of her rebuttal reports. (*See* Ex. E, Rebuttal Rep. at 4; Feigal Rebuttal Report at 2, attached as Exhibit I.) Yet, again, Dr. Betensky ignores FDA's warnings and misuses MAUDE data for the purpose of *confirming* a hypothesis that Plaintiffs' attorneys paid her to confirm, rather than to *generate* a hypothesis. (*See* Ex. C, MDL Dep. Tr., 172:18 to 173:5.) Because of the numerous limitations with the MAUDE data, FDA Guidance demands that Dr. Betensky's opinions be "viewed with extreme caution." (Ex. H, FDA Guidance at § IV(G).)

Indeed, Dr. Betensky's frank concessions about the unreliability of her calculations highlight the danger of admitting them to the jury. For example, Dr. Betensky admitted that she provided only an "estimate [that] could be an overestimate or it could be an underestimate." (Ex. B, Austin Dep. Tr., 62:16-19.) To the point, she admitted it was "not possible" for her to calculate a rate of error or "single measure of bias." (*Id.* at 112:13 to 113:7.) Dr. Betensky does not know and could not say whether confounding factors affected her analysis. (*Id.* at 110:3-7.) Moreover, her analyses do not "account for . . . potential external limitations, which can't be addressed exclusively by the numbers on the page. And so for those, there's additional error or overestimation/underestimation, and that's not part of the error that is accounted for." (*Id.* at 126:8-20.) Finally, and perhaps the most compelling reason that these opinions should be excluded, Dr. Betensky conceded that her opinion or "estimate" is "not the truth and is different in some ways from the truth." (*Id.* at 113:9-11.)

This Court should exclude Dr. Betensky's opinions because they are based entirely on her misuse of anecdotal adverse event reports made to MAUDE or Bard data "to

compare adverse event occurrence rates across devices," which the FDA has specifically warned is not how such reports are intended to be used because of the numerous limitations with such data. Admitting any such opinions would also unfairly prejudice Bard by giving the jury the misleading impression that this unreliable comparison of adverse event rates is reliable because of its presentation through an expert. Fed. R. Evid. 403.

IV. Conclusion.

For each of these reasons, Bard respectfully requests that this Court exclude the opinions of Dr. Betensky in their entirety.

RESPECTFULLY SUBMITTED this 24th day of August, 2017.

s/Richard B. North, Jr.
Richard B. North, Jr.
Georgia Bar No. 545599
Matthew B. Lerner
Georgia Bar No. 446986
NELSON MULLINS RILEY & SCARBOROUGH, LLP
Atlantic Station
201 17th Street, NW / Suite 1700
Atlanta, GA 30363
PH: (404) 322-6000
FX: (404) 322-6050
richard.north@nelsonmullins.com
matthew.lerner@nelsonmullins.com

James R. Condo (#005867)
Amanda Sheridan (#027360)
SNELL & WILMER L.L.P.
One Arizona Center
400 E. Van Buren
Phoenix, AZ 85004-2204
PH: (602) 382-6000
jcondo@swlaw.com
asheridan@swlaw.com

Attorneys for Defendants C. R. Bard, Inc. and Bard Peripheral Vascular, Inc.

CERTIFICATE OF SERVICE

I hereby certify that on this 24th day of August 2017, the foregoing was electronically filed with the Clerk of Court using the CM/ECF system which will automatically send e-mail notification of such filing to all attorneys of record.

s/Richard B. North, Jr.
Richard B. North, Jr.

Nelson Mullins Riley & Scarborough L.L.P.
201 17th Street NW, Suite 1700
Atlanta, GA 30363
(404) 322-6000